ENCYCLOPEDIA
on Early Childhood
Development

Autism: Early Development

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Introduction

Autism is a neurodevelopmental condition characterised by social communication difficulties together with restricted and repetitive behaviours and sensory sensitivities.[1] Approximately 1 in 100 children are diagnosed with autism worldwide, and there is a higher prevalence in males compared to females with a ratio of 4:1.[2] Autism often co-occurs with intellectual disability, mental health difficulties and neurodevelopmental conditions such as attention deficit/hyperactivity disorder (ADHD).

Subject

Autism diagnosis is based on observable behavioural characteristics such as reduced eye contact, lack of to-and-fro conversation, restricted and/or unusual interests and sensory hypo- and hyper-sensitivities. It is therefore not typically diagnosed until toddlerhood at the earliest. Identifying early infant markers can elucidate the neurobiological mechanisms underlying autism, as well as offering the potential to augment current screening procedures and enable earlier intervention.

Problems

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i. An over-reliance on the infant sibling design.

Twin studies have shown autism to be highly heritable.[3] In order to characterise the earliest signs of autism, longitudinal infant sibling studies follow infants who have an older brother or sister with a diagnosis. Approximately 10-20% of these infants go on to develop autism,[4] and researchers examine which factors in infancy are associated with a later diagnosis. Other study designs which enable the prospective study of autism include infants with genetic conditions (such as tuberous sclerosis complex) and pre-term infants. The aetiology of autism may be different in these populations. The majority of studies utilise an infant sibling design and findings may not be generalisable to syndromic autism.

ii. The *specificity* of infant markers to autism is often unknown.

Autism co-occurs highly with mental health conditions such as anxiety, as well as other neurodevelopmental conditions (e.g., ADHD), which means that the *specificity* of early markers cannot easily be determined. In order to understand the developmental mechanisms underlying autism, it is necessary to measure other co-occurring conditions at outcome, yet only a handful of studies to-date have taken this approach.

iii. Small sample sizes may lead to low replicability.

The study of autism, and indeed the fields of psychology and psychiatry more broadly have struggled with a replication crisis, driven in part by studies with small sample sizes. The field has tried to tackle this problem through multi-site consortia with shared protocols. However, many of the experimental biomarker studies in the field still require replication with well-powered samples.

Research Context

The early autism field is moving towards large scale consortia, combining longitudinal data across multiple levels: genetic, neural, cognitive, behavioural, etc. The strength of this design is the ability to characterise the dynamic processes underlying the emergence of autism.

Key Research Questions

- Do infants who later develop autism show early cognitive differences?
- Are there differences in early brain development in autism?

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- Does early intervention influence developmental outcomes?

Recent Research Results

Do infants who later develop autism show early cognitive differences?

Over the past decade, several cognitive markers have been associated with emerging symptoms of autism, helping to elucidate the underlying developmental mechanism.[5,6] While some studies have shown early differences in social processing (e.g., reduced attention to complex social stimuli[7]; less orienting to audio-visual synchrony displayed within biological motion[8]), others show no difference compared to typically developing infants (e.g., orienting to a face in a static display[9]; reflexively following a gaze cue[10]). 'Social first' theories propose that an early reduction in infant social attention results in a developmental cascade leading to autism. Contrary to this, studies showing a declining trajectory of social engagement[11,12], suggest that difficulties emerge, rather than being present from immediately after birth. There is also evidence for broader attentional differences, including slower attention shifting[13], stronger pupillary light reflex[14] and enhanced visual search performance[15] being associated with autism outcome.

Are there differences in early brain development in autism?

Young children with autism tend to show a larger head circumference and greater brain volume. It has been suggested that hyper-expansion of the cortex in infancy may precede brain volume overgrowth.[16] An increase in intermediate neural progenitor cells has been proposed as the mechanisms linking cortical expansion with increased brain volume and disruptions in neural connectivity.[17] The evidence for connectivity differences, however, is less clear. There is a hypothesis that autism might be linked with long-range under-connectivity and local over-connectivity.[18] However, the pattern of findings for early connectivity differences in autism remains mixed, likely dependent in part on methodological factors.[19]

Does early intervention influence developmental outcomes?

Over the past decade, there have been a number parent-mediated interventions with infants who have an elevated likelihood for developing autism. The clinical aim of such interventions is often to support children's development or longer-term outcomes, but from a basic science perspective, randomised control trial methodology also enables the causal effect of changing the early environment to be measured. Based on the evidence to-date, a recent meta-analysis

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concluded that there were clear effects for parent behaviour change but no evidence for direct effects on child behaviours.[20] However, there may be more subtle effects on child outcomes. Yoder, Stone and Edmund[21] found that increased intervention fidelity mediated a trend towards improved child outcomes. Further, a different parent-mediated intervention, showed significant cumulative effects on child autism outcomes when children were followed-up later in development.[22]

Research Gaps

i. Robust biomarkers for autism are yet to be identified.

While many early markers have been associated with autism, they do not meet the criteria for 'biomarkers'.[23] Biomarkers must be objectively, reliably, and accurately measured, and linked to the underlying biological or pathogenic process. Before progress towards clinical utility can begin, there remains a key need for replication, establishing sensitivity and specificity as well as considering the 'value-added' over-and-above questionnaires or screening tools.[24] Given the heterogeneity of autism, one exciting future potential for biomarkers is in stratifying different subgroups within autism.[25]

ii. Mechanisms of resilience are not well understood.

Resilience, which refers to those achieving 'better than expected' outcomes, is not well understood in autism.[26] The field lacks a clear framework for characterising resilience processes.

Conclusions

Infant sibling studies have identified a range of neurocognitive markers associated with later autism outcome. Characterising the trajectories of these markers has been important in understanding developmental mechanisms in autism. Differences in social processing may emerge later in development, towards the end of the first year of life, with no evidence for an initial reduction in infant attention to faces and early gaze following behaviour. This is in contrast to 'social first' theories which propose that reduced infant social attention results in a developmental cascade leading to autism. While important from a basic science perspective, the lack of evidence regarding stability and robustness of these markers means that their clinical utility has been somewhat limited. Future large-scale consortia, which aim to to replicate effects, establish the specificity of early markers to autism, and test their potential utility in stratifying

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different subgroups of autistic children will be of key importance for the field.

Implications for Parents, Services and Policy

While a decade of infant sibling research has identified early markers related to autism, there remains a need for replication across large, representative samples. For successful translation to clinical practice, it is important not only to have robust markers, but also to consider the utility of such markers over-and-above existing screening procedures. The Research Domain Criteria framework[27] emphasises the importance of taking a dimensional approach, in which a child's profile can be more fully characterised; the use of biomarkers in stratification of profiles is a key aim for future research. The fields of psychology and psychiatry more broadly are moving towards more personalised approaches. Precision medicine approaches offer the ability to test which individuals benefit most from particular intervention. In order to build towards more effective treatments, which improve outcomes for autistic children, there is a need to integrate robust trial methodology with an understanding of developmental mechanisms.

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